FY13 Priorities

Project Title: Unsolicited Investigator Initiated Renewals

Mechanism(s): R01, D43, P30, P50, R24, U01, U10, P01
Competing Renewal, New or Expansion: 100% Competing Renewal
% of Minority/International: M 35%, I 12%
Plan Objectives(s): 1A, 1B, 1C, 2A, 2B, 2C, 2D, 2E, 2G, 5A, 5B, 5C, 5D, 6A, 6B, 6C, 6D, 6F, 6G, 6J, 7A, 7B, 8A, 8B, 8C

Narrative Justification:

NIDA supports a broad range of research on the drug abuse aspects of HIV/AIDS in diverse, drug using populations to reduce the acquisition and transmission of HIV associated with sharing injection paraphernalia and/or high risk sexual behavior, to improve HIV treatment including access and utilization of services, and to reduce the consequences of HIV/AIDS. Research on drug abuse treatment as a component of HIV prevention as well as studies to enhance adherence to drug abuse and AIDS treatment and retention in drug abuse and AIDS treatment are also a significant component of NIDA's HIV/AIDS research. NIDA also supports research on the natural history, epidemiology, etiology and pathogenesis, prevention, and treatment of HIV/AIDS and AIDS-related co-infections (e.g., hepatitis B virus (HBV), hepatitis C virus (HCV), other sexually transmitted infections (STIs), and tuberculosis (TB)) and other comorbid conditions. Another research area supported by NIDA is basic research, including the use of animal models and in vitro systems to study the role of drugs of abuse in HIV/AIDS etiology and pathogenesis; neuroAIDS, genetics (host and viral genetic factors), epigenetics, proteomics, and systems biology are major areas of this program. Because HIV/AIDS associated with drug abuse knows no national boundaries, NIDA supports international research to reduce the intertwined epidemics of HIV/AIDS and drug abuse. NIDA also participates in collaborative efforts with other Institutes and Agencies in order to leverage resources and conduct complementary research.

FY 2013 Plan. This initiative is consistent with all the scientific objectives and emphasis areas in the NIH/OAR FY 2013 Trans-NIH Plan for HIV-Related Research with the exception of Emphasis Areas #3 and 4, Microbicides and Vaccines. NIDA has FOAs that address HIV/AIDS health disparities in the US, implementation, HIV prevention, and HIV/AIDS treatment for substance users. NIDA also contributes to collaborative efforts of CFARs, PHACS, ATN, HPTN, and WIHS. Through NIDA CTN, NIDA is supporting studies on retention in HIV care for HIV infected patients recruited from a hospital setting. CTN is also working with SAMHSA to develop a blending product to disseminate results from CTN0032 study on HIV testing in drug treatment centers.

Project Title: HIV Prevention in Vulnerable Populations in the U.S.

Mechanism(s): R01, R21, R03, R34
Competing Renewal, New or Expansion: Expansion
% of Minority/International: M 80%
Plan Objectives(s): 1A, 1B, 1C, 5A, 5B, 5C, 5D

Narrative Justification:

As the US AIDS epidemic has evolved; there has been a shift toward increasingly disproportionate representation of ethnic/racial minorities, particularly African-Americans and Latinos in the number of AIDS cases and numbers of new infections. There has also been a resurgence of HIV cases among men who have sex with men (MSM), particularly those who are members of ethnic/racial minority groups. Non-injection drug use, particularly use of stimulants and club drugs, has an important role in the fueling this epidemic in MSM. Therefore, a focus on combining drug abuse treatment (testing new pharmacotherapies in combination with behavioral therapies) with other interventions may hold promise in racial/ethnic MSM. Drug use and/or drug using sexual partners are also important components of the heterosexual ethnic/racial minority epidemics. Minorities are in need of better interventions for HIV prevention, with consideration of cultural and structural factors, which may account for racial/ethnic disparities. At the population level HIV treatment is HIV prevention and it is essential that minorities be engaged in HIV testing, linkage to care, and retention in ARV therapy (seek, test, treat, and retain). Even though disparities have increased over time, there often are few racial/ethnic differences in sexual risk behavior. Some of the most vulnerable populations for HIV infection do not see themselves as being at risk. Sexual networking patterns may be significant contributors to the dissemination of HIV among particular ethnic/racial groups, particularly within defined geographic areas. It is important to consider both individual factors such as co-morbidities or differential distributions of genetic risk or protective factors and contextual and socioeconomic factors. Examples of research that would further this initiative include:

- Epidemiological research which considers factors such as substances used, networking patterns, access to care & prevention, and cultural factors which may account for disparities in HIV acquisition between white and ethnic/racial minority populations.
- Research on ethnic/racial disparities in HIV acquisition that address different distributions of co-occurring disorders (e.g., STIs), different distributions of genetic risk and protective factors and other biological variables which may contribute to disparities.
- Development and evaluation of interventions to reduce HIV risk among racial/ethnic minority MSM, which take into account factors such as substances used, networking patterns, access to drug abuse treatment (especially new pharmacotherapies)combined with other preventive interventions, and cultural factors which may account disparities in HIV acquisition and transmission.
- Development and evaluation of interventions to reduce HIV risk among racial/ethnic minority women, which take into account factors such as substances used, networking patterns, access to care & prevention, exposure to violence and trauma, and cultural factors.

- Development and evaluation of interventions to reduce HIV risk among drug using MSM, which take into account factors of how sexual risk behavior may be affected by substances of choice, levels of substance use and abuse, and relationships among sexual, social, and drug use networks.
- Development and evaluation of interventions to increase HIV test uptake, linkage to care, and adherence to antiretroviral medications, and retention in care among ethnic/racial minorities, with particular attention to cultural and structural factors that may lead to delayed testing or late testing and impede antiretroviral use.
- Develop interventions for urban drug using Native American populations that provide effective and efficient outreach as well as prevention intervention, HIV testing, and linkage to care and prevention services.

FY 2013 Plan: This initiative is consistent with the NIH/OAR FY 2013 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objective A) by characterizing risk factors in vulnerable populations, (Objective B) by evaluating factors influencing uptake and adherence to all steps of the testing and treatment process, and (Objective C) by ensuring that domestic epidemiological studies accurately represents populations at risk for HIV/AIDS. This initiative also supports Behavioral and Social Science (Objectives: A, B, C, and D) in developing, evaluating, and advancing prevention interventions (at both the individual and community level); conducting basic and behavioral research on factors influencing HIV risk behaviors and on the consequences of HIV disease; conducting treatment, health, and social services research for people infected and affected by HIV; and quantitative and qualitative research to enhance HIV prevention and care. By focusing on prevention in vulnerable populations in the US, this initiative seeks to reduce disparities in disease transmission and acquisition.

Project Title: Developing Comprehensive Interventions for Substance Using MSM

Mechanism(s): R01, R34,
Competing Renewal, New or Expansion: New and Expansion
% of Minority/International: M 35%, I 10%
Plan Objectives(s):1A, 1B, 1C, 5A, 5B, 5C, 5D

Narrative Justification:

MSM continue to be disproportionately affected by HIV. CDC's current estimates indicate that HIV diagnoses among MSM are 44-86 times greater than for other men, and 40-77 times that of women in the US. In addition to ongoing transmission among MSM in the US, MSM have emerged as a population at considerable risk for HIV in parts of Asia, epidemics have re-emerged in parts of Europe, and HIV among MSM communities in Africa is beginning to be identified. Substance abuse is common among MSM both in the US and increasing in international regions such as Asia, particularly in association with MSM at elevated risk of acquisition or transmission through risky sexual behaviors. Methamphetamine use, in particular, has been identified as a driver of risk among MSM, in part because of its motivational effects on behavior. Other stimulant use is common, particularly cocaine and crack, as well as the use of "club drugs' (e.g., ecstasy), and alcohol; poly-substance use is common. Drug treatment intervention research typically has not targeted MSM and efficacious pharmacological interventions are not yet available for stimulants. Behavioral interventions have shown mixed effects; reductions in sexual risk behavior may not be sustained. There is a continuing need for new and novel interventions, including more effective pharmacological and behavioral treatments for stimulant use and specialized interventions that address episodic, poly-substance use that is associated with high risk sexual behavior Substance use, particularly stimulant abuse, has been a barrier to adherence to HIV medications, and studies are needed in MSM to determine whether substance use interferes with the effective use of medication-based pre-exposure prophylaxis (PrEP). This priority supports the development of comprehensive, multidisciplinary approach that focuses on the interdependent nature of sexual and substance use risk, as well as effects of substance use on adherence to antiretroviral treatment (ART) for HIV treatment and prevention (including PrEP). This would include behavioral and pharmacological approaches to treating stimulant dependence, integrated service delivery systems for managing drug treatment and ART.

This priority includes, but is not restricted to:

- Development and evaluation of novel behavioral and pharmacological treatments for stimulants among MSM.
- Implementation and evaluation of interventions that integrate HIV transmission prevention, substance abuse treatment, and treatment for HIV and the complications associated with HIV therapeutics into single systems of care, with attention to long-term management of co-morbidities (e.g., HCV, HBV, STIs), medical consequences and disease progression.
- Evaluation of substance use effects on PrEP and ART uptake and adherence •

- Evaluation of longitudinal patterns of drug use among MSM, with attention to how use changes between and among substances and how substance use is associated with sexual risk behaviors that facilitate HIV acquisition and transmission.
- Retrospective studies with rigorous non-experimental designs (e.g., case-control) that evaluate how substance use is managed over time by MSM, with attention to factors related to avoidance or reduction of substance to develop resilience-based interventions.

FY13 Plan; This initiative addresses disparities based on sexual identity and addresses MSM, the group in the US that bears the highest burden of HIV/AIDS.

Project Title: Implementation Science Research

Mechanism(s): R01, P50, P01, U10
Competing Renewal, New or Expansion: Expansion
% of Minority/International: M 35%, I 25%
Plan Objectives(s): 1A, 1B, 1C, 5A, 5B, 5C, 5D,

Narrative Justification:

Efficacious interventions developed to prevent or treat HIV/AIDS in a particular setting often yield disappointing results on scale-up in diverse settings. Another issue is how to choose between competing interventions. Implementation science research is the multidisciplinary field that addresses such issues. Implementation science research seeks to understand the etiology of gaps between expected results and observed outcomes. Implementation science studies the effectiveness and cost-effectiveness of interventions; its goal is the integration of research findings and evidence-based interventions into healthcare policy and practice and, hence, to improve the quality and effectiveness of prevention, treatment, health services and care. Implementation science research recognizes that the environment, economics, culture, gender, behavior, and social circumstances are all factors that may complicate adapting interventions from one setting or population to another. Because drug abuse is stigmatized and often dealt with punitively rather than from a public health perspective, implementation science research may be particularly useful in identifying barriers and testing possible solutions for HIV/AIDS interventions in drug using populations. The ultimate goal of implementation research is to determine how best to provide a comprehensive, integrated mix of high quality, sustainable interventions to reduce HIV risk behavior and infections.

Implementation gaps in the U.S. and internationally that this initiative addresses include but are not limited to:

Needle and syringe programs (NSP)—NSP are an important component of HIV/AIDS comprehensive prevention for IDU. NSP have been used as platforms to provide a variety of services to IDUs (e.g. HIV testing, condom distribution, referral to drug abuse treatment) in addition to providing sterile syringes. But there has been no systematic implementation research on NSP as comprehensive HIV prevention and treatment for IDU. Provision of medical services for IDU such as HCV testing and STD screening have all been implemented to varying degrees in NSPs, but there have not been studies on how best to integrate services and to assure continuity of care. NSPs have developed as alternative health care systems for IDUs, but whether this is optimal or whether integration into existing health care would be more cost-efficient and/or more effective or whether integration of services for IDU into standard healthcare settings would reduce the stigma associated with IDU has not been studied. NSPs have used fixed sites and mobile vans to deliver services; a better understanding of how best to deploy NSP services in particular communities is needed. Community attitudes and laws affecting NSP often impact NSP implementation. Establishing a target level of syringe distribution coverage for a given site is dependent on the epidemiologic and behavioral characteristics of the particular drug using population. Important outcome measures would include expansion of coverage, retention of NSP users, referrals to

drug abuse treatment or on-site delivery of medication assisted therapy, medical services provided and integration of services, provision of comprehensive prevention services for injection and sexual risk reduction, including education and counseling, condom distribution, etc., estimation of reduction in risk behaviors and/or HIV incidence.

ART as HIV prevention- Engaging and retaining drug users in care**:** Bringing drug users into care earlier in the course of HIV infection and retaining them in care are crucial to maximizing prevention opportunities, preserving the efficacy of first-line ART, and improving individual and population health outcomes. Examples of research topics include: 1) Testing of models to optimize coverage of care services; 2) Comparing models of service provision and adherence support; 3) Delineating key issues that result in suboptimal clinical outcomes; 4) Identifying appropriate portals for HIV testing; and 5) Identifying social and structural barriers as well as individual-level behaviors to ART initiation and maintenance.

Integrated behavioral and biomedical interventions in real world settings--To date, there are several promising integrated behavioral and biomedical treatments and approaches that have shown positive outcomes in decreasing the rate of new HIV infections, promoting greater adherence to HIV treatment and overall medical management, improving engagement and retention in HIV care, and reducing substance abuse. However, there remains a large gap regarding translation from research models into combination approaches that are effective in "real world" settings, such as front -line community based organizations, substance abuse treatment venues and other direct providers of clinical care. Maximizing adherence in the broadest sense is key to effective implementation. Specifically, this initiative seeks to explore mechanisms to successfully transfer and sustain efficacious integrated combination preventive and treatment interventions (e.g., targeting use of and adherence to HAART, screening and risk reduction, engagement and long-term maintenance in HIV care, and overall medical management for co-morbid conditions, such as substance use, mental health impairments, Hepatitis C, TB) for at-risk and HIV+ populations in real-world practice settings. This may include investigating the optimal settings and approaches for intervention delivery (primary-based care, urgent care and/or specialized care settings, home) as well as a structured analysis of local community resources to understand the capacity needed to deliver the optimal "dose" of required treatment. In short, it is critical to understand how evidence-based interventions are transported into and maintain their potency in real-world community-based practice settings (e.g., ERs, primary care, criminal justice settings, drug treatment etc.).

Opioid substitution therapy (OST) as HIV prevention-OST is unavailable or of limited availability in many settings. In the U.S., OST is limited or unavailable in criminal justice settings. In the U.S. physician adoption of buprenorphine/naloxone OST has been relatively slow due to regulatory, financial, and attitudinal barriers. Yet, because buprenorphine/naloxone can be prescribed by physicians and dispensed at community pharmacies as opposed to methadone, which usually requires daily visits to a specialized clinic, there are advantages in terms of patient acceptability. In addition, because a specialized dispensing clinic is not required, it may be easier to integrate buprenorphine/naloxone treatment with HIV care. Internationally, there are many countries with large numbers of IDUs and high HIV prevalence that have little or no OST. Implementation science research is needed on how best to

expand OST for a given setting. The use of OST as a stand-alone intervention compared with integration of OST with ART and treatment for comorbid conditions is another major area for study by implementation scientists. It will be important to determine which programs are most effective in expanding OST coverage and the relationship between OST coverage and reductions in risk behavior. In addition, studies should evaluate whether OST leads to increased adherence to HAART and improved HIV treatment success.

Long-lasting opioid pharmacotherapy with depot naltrexone—In countries that do not allow opioid agonists to be used to treat opioid addiction, intramuscular injection of extended release naltrexone can be used once a month treatment. This therapy may also be beneficial in situations where adherence is an issue and where there is few health care staff. Implementation research studies are needed on long-lasting opioid antagonists. It will be important to determine whether patients remain in treatment and to what extent they reduce their HIV risk behavior and/or maintain their adherence to HAART.

FY 2013 Plan: This initiative is consistent with the FY13 Trans-NIH Plan for HIV-Related Research Natural History and Epidemiology (Objectives A, B, and C) by supporting studies on the uptake and adherence to frequent HIV testing and linkage to and retention in care, studies on the cost-effectiveness of preventive interventions, determinants of HIV acquisition among vulnerable populations, research on substance abuse treatment modalities as HIV prevention interventions, evaluating the impact of substance abuse treatment on the effectiveness and, and consequences of ART, and encouraging more HIV prevention research in at-risk marginalized and vulnerable populations. It supports Behavioral and Social Sciences (Objectives A, B, C, D) by supporting research substance use and sexual transmission, designing and testing interventions for vulnerable populations, studying risk and protective behaviors associated with HIV transmission and progression in specific social and cultural contexts, studying barriers to health care utilization, refining techniques for measuring social networks and for collection of reliable information on sexual and drug-use risk behaviors. This initiative supports research on the feasibility, effectiveness, and sustainability required for scale-up and implementation of interventions for communities at risk in the US and internationally.

Project Title: Transformative Research

Mechanism(s): DP1, RPGs
Competing Renewal, New or Expansion: New and expansion
% of Minority/International: M, I
Plan Objectives(s):1A, 2A, 2B, 5A, 6A

Narrative Justification:

NIDA Director's Avant-Garde Award Program for HIV/AIDS Research: In FY08, NIDA introduced the Avant-Garde award to encourage cutting edge, high-risk, high payoff HIV/AIDS research that has the potential to open new avenues of research and/or have broad public health impact by leading to new breakthroughs in HIV/AIDS prevention and treatment interventions for substance users. It uses the DP1 mechanism; the same mechanism as the NIH Director's Pioneer award. This ongoing program selects 2-3 awardees each year. Avant-Garde awardees are conducting studies that are highly relevant to efforts towards a cure by focusing on strategies that may lead to new therapies to control or eliminate HIV. Among the funded projects are: studies of HIV reservoirs and latency, systems biology of immune reconstitution, proteomics of virus-host interactions, and HIV transmission between cells. Treatment as prevention in injection drug users was one of the projects funded in 2008; several significant papers have already resulted from this ward. NIDA is developing a FOA to allow continuation of the research begun under the DP1 award.

FY13 Plan: This initiative attracts extremely creative scientists who wish to pursue high-risk, high pay-off research that has the potential to transform treatment and/or prevention for drug users. It includes basic and therapeutic research focused on elimination of viral reservoirs leading toward a cure. This initiative supports emphasis areas Etiology and Pathogenesis 2A,2B, 2C and Therapeutics 6A. It also supports potentially transformative Behavioral and Social Sciences interventions 5A and Natural History and Epidemiology 1A.

Project Title: Genomics and Systems Biology Research on HIV/AIDS and Substance Abuse

Mechanism(s): RPGs
Competing Renewal, New or Expansion: New
% of Minority/International: M 5%, I 2%
Plan Objectives(s): 2A, 2B, 2C, 2D, 2G, 5B, 6A, 6G

Narrative Justification:

Technological advances in genomics, epigenomics, proteomics, transcriptomics, metabolomics, and other related approaches have allowed unprecedented generation of comprehensive data sets that may uncover a wealth of knowledge about the basis for disease. Computational approaches can be used to interrogate these data sets to identify SNPs, transcripts, molecular entities, and pathways important in a particular biological or disease process. Systems biology approaches, which include this combination of data set generation and computational analysis, have great potential to generate new and unexpected hypotheses. Together, these approaches have tremendous potential to redefine complex HIV-host interactions and to open new avenues for prevention and treatment research in HIV/AIDS and substance abuse.

Systems approaches currently are being used to identify biological pathways critical for HIV replication, potential new targets for antiretroviral treatment, factors that provide natural immunity against infection, and processes involved with viral latency and reactivation. Substance abuse researchers are exploiting systems biology approaches to identify new molecules and pathways involved in addictive processes. Strategies interrogating epigenomic, transcription factor binding, and gene expression data sets have been used to identify new and unexpected signaling pathways that regulate cocaine-taking behavior in rodents. Systems genetics approaches interrogating genetic variation, gene expression, and a suite of behavioral assays have identified quantitative trait loci and genes for a number of drug abuse relevant phenotypes. Although systems biology approaches have been independently fruitful for HIV/AIDS and substance abuse research, studies combining these areas of focus have been uncommon. This initiative is designed to generate and interrogate large data sets and stimulate the use of systems biology approaches to answer questions and generate hypotheses of significance to both HIV/AIDS and substance abuse.

Topics to be addressed with this initiative include:

1. Viral latency and reservoirs

- Impact of substance use history on establishment and persistence of latent HIV infection, long-term maintenance of latently infected cells, or the dynamics of reactivation from latency
- Effects of substance use on penetration of HIV treatment medication into anatomical reservoirs
- Identification of targets and/or small molecule modulators with the potential to eliminate HIV reservoirs or otherwise lead to a cure for HIV infection in the context of substance abuse

2. Host immune and inflammatory responses

- Immunological mechanisms of HIV control and variation of this control throughout the course of infection
- Mechanisms of chronic immune activation or inflammation, and the impact in pathogenesis in the context of substance abuse
- Identification of molecular networks or signatures that impact HIV/AIDS phenotypes (e.g. long term non-progressors, highly exposed seronegative individuals, rapid progressors, development of neurocognitive impairment or other complications) and studies to examine whether substance use affects these signatures
- Definition of immunological parameters and molecular signatures that predict efficacy of HIV vaccine candidates or novel treatment strategies, and modifications of these parameters by substance abuse
- Impact of substance use history or treatment on immune recovery response to antiretroviral treatment regimens or immune reconstitution inflammatory syndrome (IRIS)

3. Viral determinants of pathogenesis

- Effect of non-structured antiretroviral treatment interruption (e.g., associated with poor adherence resulting from substance use relapse) on viral evolution, recombination, drug resistance or viral-host interactions involved in disease progression
- Dynamics of HIV transmission and evolution within substance using populations
- Biology of HIV infection and evolution associated with injection or non-injection substance use

4. Neurologic and other medical consequences

- Identification of factors that predict susceptibility to HIV infection in the central nervous system, neurocognitive impairment, or peripheral neuropathy in substance users
- Neural-glial and neural-immune interactions that impact progression of neural dysfunction in the HIV-infected central nervous system, and contribution of substance use or addiction to pathogenesis
- Elucidation of factors related to vulnerability and resistance to co-morbidities or co-infections (including HCV or TB) in substance using HIV-infected populations, including pharmacological, physiological, genetic, and clinical factors
- Identification of targets and/or novel medical interventions for drug abuse and co-morbid clinical conditions associated with HIV/AIDS

FY 2013 Plan: This initiative is consistent with the NIH/OAR FY 2013 Trans-NIH Plan for HIV-Related Research for Etiology and Pathogenesis (Objectives: A, B, C, D, and G) by addressing the host and viral factors involved in the transmission, establishment, and progression of HIV disease, including neurological disease, in drug-using populations. This initiative also addresses drug abuse associated risk behavior in emphasis area Basic Behavioral and Social Science Research (objective 5B). Objectives 6A, development of HIV treatments, and 6G, development of AIDS-related neurologic disease therapeutics in emphasis area Therapeutics are also addressed.

Project Title: Pharmacotherapies for HIV/AIDS in Drug Abusing Populations

Mechanism(s): RPGs
Competing Renewal, New or Expansion: Expansion
% of Minority/International: M 35%, I 10%
Plan Objectives(s): 6A-6D, 6G, 6J

Narrative Justification:

The goal of this initiative is to encourage research on pharmacotherapies for HIV and co-occurring infections including HCV, TB and others in drug abusing/dependent populations. This initiative will solicit applications to conduct clinical and preclinical research that will evaluate: (1) the impact of currently available or in-development antiretroviral medications for HIV and HCV that could be used effectively in methadone or buprenorphine-maintained drug abusing populations; (2) HIV and other co-occurring infectious disease progression in drug abusing populations; (3) the efficacy of anti-viral medications in drug abusing populations; (4) the medical safety of concurrent administration of anti-infective and antiviral medications among drug addicts; (5) possible adverse interactions between anti-infective and antiretroviral medications in drug abusing population, and (6) develop drug delivery systems for both HIV infected and drug dependent patients. This FOA will focus on drug using vulnerable populations such as women, ethnic minorities, and those vulnerable for acquiring/transmitting HIV and other infection. NIDA also participates in collaborative efforts with other Institutes and Agencies in order to leverage resources and conduct complementary research.

FY 2013 Plan: This initiative is consistent emphasis area Therapeutics in the NIH/OAR FY 2013 Trans-NIH Plan for HIV-Related Research as it pertains to treatment of HIV and coinfections in drug using populations.

Project Title: Technology-driven Strategies to Improve Assessment and Adherence

Mechanism(s): R01, R34, R03
Competing Renewal, New or Expansion: Expansion
% of Minority/International: M 30%, I 5%
Plan Objectives(s): 5A, 5B, 5C, 5D, 6B, 6D

Narrative Justification:

Maintaining drug abuse treatment and highly active anti-retroviral therapy (HAART) are important to addressing HIV/AIDS among drug abusers. Relapse to active drug use is often associated with non-adherence or lapses in ART. This priority examines the feasibility of utilizing and disseminating technologically-driven indices of assessment and adherence (e.g., Ecological Momentary Assessment (EMA), Medication Event Monitoring System, cell phone and/or Digital Assistant Device among others) in the context of delivering treatments to individuals with substance abuse disorder and HIV. There is a growing literature on the use technologies in order to monitor adherence to HAART among HIV+ populations (although not typically including HIV+ active drug users). In addition, there is some emerging data that some of these technologies, such as EMA and electronic diary reports, can be used in the context of treatment for drug-abusing populations, specifically in the recording of real-time cue exposure, cravings, and mood in the hours before cocaine and/or heroin use. As such, the use of technological instrumentation that can assess/monitor behavior and adherence in "real time" offers an innovative approach to target the multiple treatment needs, including adherence to HIV treatment regimens, monitoring of antecedent targets to drug use and/or other HIV-risk behaviors of drug-abusing populations with HIV.

Given the high rates of HIV among active drug users, the high rates of nonadherence with treatment regimens for chronic illnesses (such as HIV) as well as the optimal levels of adherence necessary to maintain virological suppression and avoid the development of anti-retroviral drug resistance, there is a critical need to develop interventions that significantly enhance adherence to HIV treatment regimens and decrease HIV-risk behaviors (e.g., sharing needles). The development of several technological measures might offer promise to address the clinical needs of the underserved population of substance users with HIV.

There are some promising interventions that use technology. This initiative also encourages the use of mobile technologies to deliver treatments targeting adherence and retention in care for which there is extant promising pilot or efficacy data for HIV-related outcomes. Mobile technologies allow for the deployability and extension of delivery of treatments to broad populations at risk. A major focus will be on particularly vulnerable populations, especially injection-drug abusing individuals with HIV, and can be executed within the US or internationally.

The topics to be addressed by this initiative include:

1. How feasible is it to develop, utilize, implement, and/or disseminate these technologies among drug abusing populations with HIV? What potential barriers exist to adopting these approaches to this population and what resources/approaches are needed to overcome those barriers?
2. Which groups and approaches are the most likely candidates for efficacious use of these technologies? What subgroups of drug-abusing populations with HIV (e.g., prisoners leaving correction facilities and transitioning back to communities; those already receiving specific behavioral and/or other interventions (e.g., DOT)) are most suitable?
3. What secondary benefits and innovative applications (e.g., HIV prevention) may be developed for and as a result of adherence-related technologies?

FY 2013 Plan: This initiative is consistent with the NIH/OAR FY 2013 Trans-NIH Plan for HIV-Related Research for Behavioral and Social Science research (Objectives: A, B, C, and D) behavioral and social science research will be investigate the use of technology to encourage drug users to adhere to treatment intervention regimens, including adherence to HAART therapy and Therapeutics (Objective B and D) by supporting studies to improve adherence to ARV regimens and regimens to treat coinfections.

Project Title: Use of Incentives and Other Strategies to Improve HIV/HCV Testing, Adherence to Medications, and Retention in Treatment

Mechanism(s): R01, R21, R34
Competing Renewal, New or Expansion: Expansion
% of Minority/International: M 40%, I 5%
Plan Objectives(s): 5A, 5B, 5C, 5D, 6B, 6D

Narrative Justification:
Evidence for HIV Treatment as Prevention (TasP) in diverse populations is accumulating. The recent availability of improved therapies for HCV suggest that a similar strategy may work to prevent HCV transmission by testing and treating those with HCV mono-infection and HCV/HIV dual infection.

TasP is critically dependent on identifying those who are infected, linking them to care, and ensuring adherence to treatment, and retention in treatment. At each stage of the process incentives and other interventions may be useful. The use of motivational incentives, or "contingency management" as it is commonly called, is one of the most powerful interventions known to promote abstinence from drugs and to promote adherence to medications to treat drug abuse. Incentives have also been used to engage and retain drug users in drug abuse treatment. This initiative encourages the use of motivational incentives as a component of the continuum of HIV prevention and treatment including HIV testing, engagement in HIV treatment, adherence to HIV treatment regimens, and retention in HIV care. Testing of TasP for HCV is encouraged in studies of populations of drug users who have a high prevalence of HIV/HCV coinfection.

A large number of drug abusers are HIV positive due to the increased risk of HIV from drug use associated with drug injection and/or high risk sexual behavior. Many HIV positive individuals are unaware of their serostatus because they have not been recently tested for HIV. The use of incentives may encourage drug using individuals at high risk for HIV to be tested for HIV at more frequent intervals and to participate in risk reduction counseling. This will enable these individuals to initiate treatment earlier in the course of their HIV disease and to modify their behavior to reduce the risk of transmitting HIV to others. To ensure treatment initiation, different strategies may be tested; these include incentives, use of peer navigators, and case management.

Highly active antiretroviral therapy (HAART) is effective in decreasing viral load to undetectable levels, but people must adhere to their HAART medication in order for the medication to be optimally effective. Poor adherence affects the individual's prognosis and may lead to the development viral resistance. Incentives may be a useful and cost effective means of improving HAART adherence in substance abusers. Although a handful of small randomized interventions trials have demonstrated promising success in increasing adherence to HIV medications through the use of behavioral interventions, such as contingency management and mDOT (modified Directly Observed Therapy), the feasibility and cost-

effectiveness of scaling up such interventions is unclear. In addition, interventions must be sustainable over the long term. Specifically, tailoring and evaluating community-friendly interventions is critical, given the financial constraints faced by resource-limited community-based clinics and treatment centers. In addition to issues of poor adherence to HAART, drug abusers frequently drop out of AIDS treatment altogether. Strategies based on behavioral reinforcement may also be of value in retaining drug users in AIDS treatment and encouraging them to access related services. Peer navigators and case management may also be used to increase adherence and retention. Studies are needed to compare different interventions and combinations of interventions in different populations in order to optimize cost-effective interventions.

The topics to be addressed by this initiative include:

- Assess what factors, information, and incentives would be necessary to motivate high-risk drug-using populations to understand the benefits of early detection of blood-borne viruses (HCV and HIV) and to undergo voluntary counseling and testing.
- Assess whether the use of incentives to maintain subjects in drug abuse treatment enhances engagement in HIV testing, linkage to HIV care, and retention in care.
- Assess whether drug abuse treatment enhances initiation, adherence, and retention in HIV treatment.
- Study how to effectively use incentives and other motivational factors to enhance HIV testing, entrance into HIV care, adherence to HAART and other treatment medication regimens, and retention in HIV treatment. Evaluate the subject characteristics (e.g., type and frequency of drug use), characteristics of the incentives program (e.g., individual or group contingency management; size and frequency of incentives), and other factors that influence effectiveness.
- Develop, implement and evaluate community-friendly interventions to promote: HIV testing, HIV treatment engagement, adherence to HAART and relevant HIV care, and retention in HIV treatment among substance abusing populations in resource-limited settings (e.g., community or clinic-based treatment centers).
- Develop strategies to maintain HAART adherence long term following cessation of mDOT or voucher incentive programs.
- Evaluate cost effectiveness of interventions using incentives across different populations and different schedules of reinforcement.
- Evaluate cost effectiveness of interventions (incentives, case management, peer navigators, and combinations of interventions).

FY 2013 Plan: This initiative is consistent with the NIH/OAR FY 2013 Trans-NIH Plan for HIV-Related Research for Behavioral and Social Science research (Objectives: A, B, C, and D) and Therapeutics (Objective B and D) emphasis areas. Basic behavioral and social science research will be investigate the use of incentives to encourage drug users to access HIV/HCV testing and counseling services, return for follow-up diagnostic results, and enter and adhere to prevention and treatment intervention regimens, including adherence to HAART and HCV therapy. Studies will investigate adherence and self-management for ARV and coinfection treatment regimens.

Project Title: Training, Infrastructure, and Capacity Building

Mechanism(s): RPGs, training
Competing Renewal, New or Expansion: Expansion
% of Minority/International: M 20%, I 7%
Plan Objectives(s): 7A, 7B

Narrative Justification:

INVEST Fellowship Program and Humphrey Fellowship Program: The INVEST program brings foreign postdoctoral fellows to the U.S. for one year of research training and also includes professional development activities and grant-writing guidance. NIDA has added additional slots to this program dedicated to training investigators with an interest in HIV/AIDS research. This expansion of the INVEST program complements other efforts by NIDA to increase international research on HIV/AIDS. The Humphrey program is a partnership with the U.S. Department of State to support a unique training program for midcareer drug abuse professionals; some of NIDA's Humphrey fellows have an interest in HIV/AIDS. In addition, NIDA participates in the national Humphrey Fellowship seminar and has organized sessions focusing on HIV/AIDS and invited participation of fellows from Emory Humphrey Program, which has an HIV/AIDS concentration. Through contacts with NIDA staff, further interactions between foreign HIV/AIDS researchers and U.S. investigators have been facilitated.

IAS/NIDA Fellowships in HIV and Drug Abuse: This joint International AIDS Society/NIDA program was initiated in FY09 and provides support for up to 4 fellows at either the junior fellow level (18 months post-doctoral training) or the senior fellow level (eight months professional development) to receive training at leading institutes excelling in research in the HIV-related drug use field.

A-START: To facilitate the entry of newly independent and early career investigators into the area of AIDS research, NIDA has developed the AIDS-Science Track Award for Research Transition (A-START) mechanism. This program supports feasibility studies using the R03 mechanism and providing up to $100,000 direct costs for two years to facilitate the entry of new investigators into drug abuse and HIV/AIDS research.

Research Training: This program supports research efforts through institutional training research grants (T32), pre-doctoral (F31), post-doctoral (F32) mechanisms. The NIDA Research Education Program for Clinical Researchers and Clinicians (R25) also supports careers as clinical researchers, clinicians/service providers, or optimally, a combination of the two and includes HIV/AIDS as a topic of interest. NIDA's Diversity-promoting Institutions Drug Abuse Research Program (DIDARP) (R24) also strongly encourages HIV/AIDS studies. To increase the numbers of underrepresented minorities in research careers in drug abuse research, including HIV/AIDS, NIDA supports a program of diversity supplements at the pre-doctoral, post-doctoral, and investigator level to train minority investigators in HIV/AIDS research. The purpose of all of these programs is to help ensure that a diverse and highly trained workforce is

available to assume leadership roles related to the Nation's biomedical and behavioral research agenda in the areas of substance abuse and HIV/AIDS.

FY 2013 Plan: This initiative is consistent with the NIH/OAR FY 2013 Trans-NIH Plan for HIV-Related Research for Training, Infrastructure, and Capacity Building (Objectives A and B) by supporting predoctoral, postdoctoral, and advanced research training across a broad range of AIDS-related disciplines. It is also consistent with the goal of establishing and maintaining the appropriate infrastructure needed to conduct HIV research domestically and internationally.